REMARKS

Claims 1 – 20 and 22 – 43 are pending in the application. However, claims 9, 18, and 29 have been previously withdrawn. Thus, claims 1 – 8, 10 – 17, 19 – 28, and 30 – 43 are currently under examination. Claims 1-3, 6-8, 10-12, 15-17, 19, 21-23, 26-28, and 31-43 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over WO 03/004599 A2 to Peleg et al. ("Peleg") in view of the journal publications of Matsuda et al. ("Matsuda"), or Ishii et al. ("Ishii"), or Kim et al. ("Kim"), for the reasons described in the previous Office Action. Claims 4, 5, 13, 14, 24, and 25 also stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Peleg in view of Matsuda, Ishii, or Kim, and further in view of WO 01/057217 to Kwon et al. ("Kwon"). Claims 16, 27, 42, and 43 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claims 1-8, 10-17, 19, 20, 22-28, and 30-43 are newly rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. All rejections and objections are respectfully traversed. Reconsideration and favorable action are requested in light of the foregoing amendments and the following remarks.

Claims 1, 10, and 20 are amended to more particularly point out and distinctly define the claimed subject matter. Claims 6, 8, 15, 17, 26, and 28 are amended to remove the parenthesis and eliminate redundancy. Claims 16, 27, 42, and 43 are amended to specify that the first and second nucleotides are operatively linked from the same promoter. Support for the amendments may be found on page 23 of the specification (description of plasmid pMG414). Claims 42 and 43 are amended to provide antecedent basis for all terms in the claims. Claims 1, 10, 20, 42, and 43 are also amended to rectify minor grammatical errors. No new matter is added into the case by the amendments.

Applicants would like to thank Examiner Leavitt for the courtesy of a telephone interview on Wednesday, October 28, 2009. The substance of the interview is that Examiner Leavitt first clarified the nature of the indefiniteness rejection of claims 1, 10, 20, 42, and 43. It was agreed that amending the claims to read "so that" instead of "in such a way that" would overcome the rejection. The art rejections were also discussed. It was agreed that claims in the present application distinguish over the prior art, specifically Peleg, because Applicants claim use of a single signal sequence for both periplasmic targeting and proteolytic cleavage recognition. In contrast, Peleg uses both a virally derived TAT sequence for periplasmic targeting and a second

bacterial signal sequence for proteolytic cleavage recognition. Both sequences are necessary to Peleg; hence, there would be no suggestion from Peleg that any sequence other than TAT would be successful for periplasmic targeting of the polypeptide. Therefore, any combination of references based on Peleg would necessarily require the TAT signal sequence and a second bacterial signal sequence. Examiner Leavitt suggested that amending the independent claims to expressly require only the single signal sequence of the GAC gene of *P. diminuta* to perform both functions in the present invention would overcome the obviousness rejection. The Examiner also mentioned that reciting the sequence identifier and listing the actual sequence in the claims is unnecessary and redundant, and that it is better to only recite the sequence identifier.

Finally, Applicants would like to express their appreciation to the Examiner for her helpful cooperation exhibited during the interview in working with Applicants to advance this case to allowance, and also her withdrawal of the previous rejection of Claims 10 and 43.

A. Claims 1-3, 6-8, 10-12, 15-17, 19, 22-23, 26-28, and 30-43 Patentably Distinguish Over The Cited References.

Claim 1 is directed to an expression vector which comprises, among other things, a polynucleotide which encodes a heterologous fusion protein. The fusion protein includes a single signal sequence of the gac gene of *Pseudomonas diminuta* (hereinafter "*P. diminuta*") and a polypeptide of interest, other than the polypeptide encoded by the gac gene of *P. diminuta*. The signal sequence and the polypeptide of interest are linked in such a way that, upon expression of the polynucleotide as a fusion protein in a suitable host cell, the signal sequence is cleaved from the fusion protein and the polypeptide of interest is released into the periplasm of the host cell. In other words, the claimed signal sequence is both a periplasmic targeting sequence and a proteolytic cleavage recognition site.

Claim 10 is directed to a prokaryotic host cell which, among other things, is stably transformed by reason of the claimed expression vector. Claim 20 is directed to a process for making a polypeptide using a prokaryotic host cell as described transformed using such an expression vector, in accordance with claim 10. Claims 42 and 43, respectively, are independent claims directed to a prokaryotic host cell transformed with an expression vector which is compatible with the host cell, as described above, and a process for production of a polypeptide of interest, also as previously described.

The Office Action cites various portions and combinations of four references which are said to show that Applicants' claims would have been obvious to a person having ordinary skill in the art. However, as discussed above, and during the interview, Peleg, said to be the "primary" reference, does not teach, disclose, or suggest an expression vector that comprises a polynucleotide sequence that codes for a fusion protein which includes the claimed single signal sequence of the gac gene of *P. diminuta*.

Peleg deals with making a fusion polypeptide by introducing an expression construct containing a viral-derived TAT signal peptide (for periplasmic targeting of the polypeptide) plus a bacterial signal peptide (for proteolytic cleavage recognition). Cited in combination with Peleg are Matsuda, Ishii, and Kim. However, the references do not describe production of a polypeptide of interest, other than the gac gene of *P. diminuta*, as specifically called for in the claims. Instead, they pertain to various disparate genetic and molecular biological characterizations of the gac gene in some species of *Pseudomonas*, and of the expression of gac protein in *E. coli*. Nothing in these references reveals any motivation or suggestion to modify Peleg, or otherwise combine the references in a manner so as to make a fusion protein marrying two polynucleotides as called for in the claims.

In response to Applicants' previous arguments, the most recent Office Action maintained that it would have been obvious to use the gac signal sequence, said to be described in Matsuda, Ishii, and/or Kim, as a substitution for the virally-derived TAT signal sequence plus the bacterial signal sequence of Peleg in an expression vector in order to produce a polypeptide of interest according to Applicants' claims.

However, the mere mention of the gac gene signal sequence in Matsuda, Ishii, or Kim, in entirely different contexts from that of the present invention, cannot reasonably be said to motivate a person of skill to attempt to reconfigure Peleg to make Applicants' invention as claimed. Again, Peleg teaches using the TAT sequence for periplasmic targeting, and requires an additional bacterial proteolytic cleavage recognition sequence. As was acknowledged by the Examiner during the October 28, 2009 interview, Peleg requires the use of the TAT lead sequence to achieve periplasmic expression, and the bacterial proteolytic cleavage recognition sequence to express only the desired polypeptide. Nothing in Peleg suggests that any construction not having the TAT sequence (such as the claimed construction having a single signal sequence of the gac gene of *P. diminuta*) would be effective in expressing a protein of

interest into periplasm according to Applicants' claims. In other words, Peleg teaches that the TAT-derived sequence is the periplasmic signaling sequence, and the bacterial signal sequence is a protease recognition sequence. (Peleg, Page 27, Line 20 through Page 30, Line 21). No art teaching is pointed to that could reasonably be said to lead a person of ordinary skill in the art to reconfigure the structure of Peleg in the manner of Applicants' claimed structure.

Accordingly, independent claims 1, 10, 20, 42 and 43 patentably distinguish over the cited combinations of references, and the rejection of those claims should not be maintained.

Claims 2-3 and 6-8 depend from claim 1, claims 11-12, 15-17, and 19 depend from claim 10, and claims 21-23, 26-28, and 30-41 depend from claim 20. The dependent claims add further elements and limitations to those of the base claims. It is well-settled that all otherwise proper claims dependent on patentable independent claims are also patentable, by definition, since the dependent claims define more features and aspects of embodiments of more broadly defined subject matter that already patentably distinguishes over the prior art. Since independent claims 1, 10, 20, 42 and 43 have been shown to patentably distinguish over cited art, all claims dependent thereon should also be allowed. Hence, reconsideration and allowance of claims 1-3, 6-8, 10-12, 15-17, 19-20, 22-23, 26-28, and 30-43 are respectfully requested.

B. Claims 4, 5, 13, 14, 24, and 25 are Patentably Distinct Over the Cited References.

Claims 4, 5, 13, 14, 24, and 25 are dependent claims that stand rejected as allegedly obvious from Peleg combined with Matsuda, Ishii, or Kim, and further combined with Kwon. However, as discussed in part A above, it has not been shown that one of skill in the art would be motivated to assemble and then attempt to combine and reconfigure various isolated aspects/ parts of Peleg, Matsuda, Ishii, and Kim in an effort to arrive at the claimed invention. But, even if there was some reason or motivation to combine aspects/ parts of these references as imagined, and there is not, there is still no further teaching, suggestion, or disclosure within Kwon or otherwise that would have led one of skill in the art to try to make the invention of the subject claims.

Kwon is directed toward the expression, in *E. coli*, of a heterologous fusion protein comprising an *E. coli* heat stable enterotoxin II signal sequence in combination with a polypeptide. Once again, Applicants do not claim to have invented the concept of a recombinant "fusion protein." But nothing about Kwon's disclosure of a special fusion protein including *E.*

coli heat stable enterotoxin II would have suggested a fusion protein as claimed by Applicants containing a single signal sequence for the gac gene and a polypeptide of interest that, upon expression of the polynucleotide, would cause a cleavage of the gac signal sequence and release of the polypeptide of interest into the cell periplasm. Unaware of Applicants' invention, a person of ordinary skill reading Kwon (and assuming for the sake of argument, also aware of the other cited references) would have no reason to attempt to fashion a fusion protein expression system for producing a polypeptide of interest according to Applicants' claims. The mere fact that Kwon discloses hIFNα-2a and hIFNα-2b as a polypeptide of interest in one expression system suggests nothing about the performance of those proteins in other expression systems, or makes any suggestion as to what, if any, alternative expression system might be suitable, and certainly nothing along the lines of Applicants' expression system.

Accordingly, a person of ordinary skill in the art reading Peleg, Matsuda, Ishii, Kim, together with Kwon would have no "obvious" reason to attempt to selectively combine and reconfigure parts of the cited references to arrive at the present claims. Therefor, reconsideration and allowance of claims 4, 5, 12, 14, 24, and 25 are respectfully urged.

C. Claims 16, 27, 42, and 43 Are Not Indefinite.

As mentioned above, claims 16, 27, 42, and 43 stand rejected as allegedly indefinite for failing to specify how the first and second polynucleotide are operatively linked. The claims have been amended as agreed to in the interview to recite that the two nucleotides are expressed under the control of a single promoter region, as described on page 23 of the Specification (description of plasmid pMG414). Accordingly, any alleged indefiniteness of the claims has been rectified, and reconsideration and allowance of claims 16, 27, 42, and 43 are respectfully requested.

D. Claims 1-8, 10-17, 19, 20, 22-28, 30-43 Are Not Indefinite.

Claims 1, 10, 20, 42, and 43 also stand rejected as allegedly indefinite by reason of the phrase "such as" ("in such a way that"), and claims 2-8, 9-17, 22-28, and 30-41 are rejected as depending from one or more allegedly indefinite claims. The subject claims have been amended to replace "in such a way that" with "so that" in accordance with the Examiner's suggestion.

Hence, any alleged indefiniteness problems with claims 1-8, 10-17, 19, 20, 22-28, and 30-41 due to the phrase in question have been rectified.

Claims 42 and 43 are additionally rejected as allegedly indefinite due to an alleged lack of antecedent basis for certain recited terms. The claims are hereby amended to rectify any asserted antecedent basis issues with regard to the subject terms.

Claim 42 was also rejected as allegedly indefinite due to the phrase "wherein the host cell is stably transformed by the expression vector." However, this phrase is not found within the claim. Therefore this rejection appears to be in error, and Applicants request clarification and/or that this rejection be withdrawn.

Accordingly, the above-mentioned claims no longer contain any wording or phraseology believed by the Examiner to render them indefinite. Withdrawal of all Section 112 rejections is therefore proper and called for. Reconsideration and allowance of Claims 1-8, 10-17, 19, 20, 22-28, 30-43 are hereby respectfully requested.

E. The Objections to Claims 6, 8, 15, 17, 26, and 28 Are Overcome.

Finally, claims 6, 8, 15, 17, 26, and 28 were objected to as allegedly redundant for reciting both descriptions of the nucleotide sequences and sequence ID number. The claims were also objected to for including such identifiers in parenthesis. The claims have been amended to rectify any alleged redundancies and punctuation errors. Accordingly, the objections to the claims are overcome. Reconsideration and withdrawal of the objections to Claims 6, 7, 15, 17, 26, and 28 are hereby respectfully requested.

CONCLUSION

Applicants assert that the specification and claims of the present application meet the requirements of 35 U.S.C. §§112, 102, and 103, and that the claims patentably distinguish from the cited references. Applicants respectfully submit that a full and complete response to the office action is provided herein sufficient to advance the case, and that the application is now fully in condition for allowance. Action in accordance therewith is respectfully requested.

In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our Deposit Account No. 12-2355.

Respectfully submitted,

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